VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

Claims 57, 73, 88-98 and 103 have been cancelled.

Claims 55, 56, 58-60, 62-67, 69-72, 74, 75, 78-82, 85-87 and 99-102 have been amended as follows.

55.   (Amended) A method of defining a set of compounds [that modulate the expression of a target nucleic acid sequence via binding of said compounds with said target nucleic acid sequence] comprising:

generating *in silico* virtual compounds according to [defined criteria] thermodynamic property, target accessibility, targeting to functional regions of target nucleic acid sequence, or uniform distribution to target nucleic acid sequence, wherein said virtual compounds modulate the expression of [said] a target nucleic acid sequence;

synthesizing compounds corresponding to at least some of said virtual compounds; and

robotically assaying said synthetic compounds for one or more desired physical, chemical or biological properties by computer-controlled [real-time] polymerase chain reaction or by computer-controlled enzyme-linked immunosorbent assay.

56.   (Amended) A method of defining a set of compounds [that modulate the expression of a target nucleic acid sequence via binding of said compounds with said target nucleic acid sequence] comprising:

evaluating *in silico* a plurality of virtual compounds according to [defined criteria] thermodynamic property, target accessibility, targeting to functional regions of target nucleic acid sequence, or uniform distribution to target nucleic acid sequence; and

robotically assaying a plurality of synthetic compounds corresponding to at least some of said virtual compounds for one or more desired physical, chemical or biological properties by computer-controlled [real-time] polymerase chain reaction or by computer-controlled enzyme-linked immunosorbent assay.

58.   (Amended) A method of defining a set of compounds [that modulate the expression of a target nucleic acid sequence via binding of said compounds with said target nucleic acid sequence] comprising:

generating a library of nucleobase sequences *in silico* according to [defined criteria] thermodynamic property, target accessibility, targeting to functional regions of target nucleic acid sequence, or uniform distribution to target nucleic acid sequence; and

robotically assaying a plurality of synthetic compounds having at least some of said nucleobase sequences for one or more desired physical, chemical or biological properties by computer-controlled [real-time] polymerase chain reaction or by computer-controlled enzyme-linked immunosorbent assay.

59.   (Amended) A method of defining a set of compounds [that modulate the expression of a target nucleic acid sequence via binding of said compounds with said target nucleic acid sequence] comprising:

evaluating *in silico* a plurality of virtual compounds according to defined criteria, wherein said defined criteria is thermodynamic property, target accessibility, targeting to functional regions of target nucleic acid sequence, or uniform distribution to target nucleic acid sequence; and

robotically assaying a plurality of synthetic compounds corresponding to at least some of said virtual compounds for one or more desired physical, chemical or biological properties.

60.   (Amended) A method of generating a set of oligonucleotides [that modulate the expression of a target nucleic acid sequence via binding of said oligonucleotides with said target nucleic acid sequence] comprising:

a) generating a library of nucleobase sequences *in silico* according to [defined criteria] thermodynamic property, target accessibility, targeting to functional regions of target nucleic acid sequence, or uniform distribution to target nucleic acid sequence, wherein said oligonucleotides modulate the expression of a target nucleic acid sequence via binding of said oligonucleotides with said target nucleic acid sequence;

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b) evaluating *in silico* a plurality of virtual oligonucleotides having the nucleobase sequences of a) according to defined criteria; and

c) robotically assaying a plurality of synthetic oligonucleotides corresponding to at least some of said virtual oligonucleotides for one or more desired physical, chemical or biological properties by computer-controlled [real-time] polymerase chain reaction or by computer-controlled enzyme-linked immunosorbent assay.

62.   (Amended) A method of generating a set of oligonucleotides [that modulate the expression of a target nucleic acid sequence via binding of said oligonucleotides with said target nucleic acid sequence] comprising:

a) generating a library of nucleobase sequences *in silico* according to [defined criteria] thermodynamic property, target accessibility, targeting to functional regions of target nucleic acid sequence, or uniform distribution to target nucleic acid sequence;

b) robotically synthesizing a plurality of synthetic oligonucleotides having at least some of said nucleobase sequences; and

c) robotically assaying said plurality of synthetic oligonucleotides for one or more desired physical, chemical or biological properties by computer-controlled [real-time] polymerase chain reaction or by computer-controlled enzyme-linked immunosorbent assay.

63.   (Amended) A method of generating a set of oligonucleotides [that modulate the expression of a target nucleic acid sequence via binding of said oligonucleotides with said target nucleic acid sequence] comprising:

a) evaluating *in silico* a plurality of virtual oligonucleotides according to [defined criteria] thermodynamic property, target accessibility, targeting to functional regions of target nucleic acid sequence, or uniform distribution to target nucleic acid sequence;

b) robotically synthesizing a plurality of synthetic oligonucleotides corresponding to at least some of said virtual oligonucleotides; and

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c) robotically assaying said plurality of synthetic oligonucleotides for one or more desired physical, chemical or biological properties by computer-controlled [real-time] polymerase chain reaction or by computer-controlled enzyme-linked immunosorbent assay.

64.   (Amended) A method of generating a set of oligonucleotides [that modulate the expression of a target nucleic acid sequence via binding of said oligonucleotides with said target nucleic acid sequence] comprising:

a) generating a library of nucleobase sequences *in silico* according to [defined criteria] thermodynamic property, target accessibility, targeting to functional regions of target nucleic acid sequence, or uniform distribution to target nucleic acid sequence;

b) evaluating *in silico* a plurality of virtual oligonucleotides having the nucleobase sequences of a) according to [defined criteria] thermodynamic property, target accessibility, targeting to functional regions of target nucleic acid sequence, or uniform distribution to target nucleic acid sequence;

c) robotically synthesizing a plurality of synthetic oligonucleotides corresponding to at least some of said virtual oligonucleotides; and

d) robotically assaying said plurality of synthetic oligonucleotides for one or more desired physical, chemical or biological properties by computer-controlled [real-time] polymerase chain reaction or by computer-controlled enzyme-linked immunosorbent assay.

65.   (Amended) A method of generating a set of oligonucleotides [that modulate the expression of a target nucleic acid sequence via binding of said oligonucleotides with said target nucleic acid sequence,] comprising:

a) generating a library of nucleobase sequences *in silico* according to [defined criteria] thermodynamic property, target accessibility, targeting to functional regions of target nucleic acid sequence, or uniform distribution to target nucleic acid sequence;

b) choosing an oligonucleotide chemistry;

c) robotically synthesizing a set of synthetic oligonucleotides having said nucleobase sequences of step a) and said oligonucleotide chemistry of step b);

d) robotically assaying said set of synthetic oligonucleotides of step c) for a physical, chemical or biological activity by computer-controlled [real-time] polymerase chain reaction or by computer-controlled enzyme-linked immunosorbent assay; and

e) selecting a subset of said set of synthetic oligonucleotides of step c) having a desired level of physical, chemical or biological activity in order to generate said set of compounds.

66.   (Amended) A method of generating a set of oligonucleotides [that modulate the expression of a target nucleic acid sequence via binding of said oligonucleotides with said target nucleic acid sequence,] comprising:

a) generating a library of nucleobase sequences *in silico* according to [defined criteria] thermodynamic property, target accessibility, targeting to functional regions of target nucleic acid sequence, or uniform distribution to target nucleic acid sequence;

b) choosing an oligonucleotide chemistry;

c) evaluating *in silico* a plurality of virtual oligonucleotides having the nucleobase sequences of a) and the oligonucleotide chemistry of b) according to [defined criteria] thermodynamic property, target accessibility, targeting to functional regions of target nucleic acid sequence, or uniform distribution to target nucleic acid sequence, and selecting those having preferred characteristics, in order to generate a set of preferred nucleobase sequences;

d) robotically synthesizing a set of synthetic oligonucleotides having said preferred nucleobase sequences of step c) and said oligonucleotide chemistry of step b);

e) robotically assaying said set of synthetic oligonucleotides of step (d) for a physical, chemical or biological activity by computer-controlled [real-time] polymerase chain reaction or by computer-controlled enzyme-linked immunosorbent assay; and

f) selecting a subset of said set of synthetic oligonucleotides of step d) having a desired level of physical, chemical or biological activity in order to generate said set of oligonucleotides.

67.   (Amended) A method of generating a set of oligonucleotides [that modulate the expression of a target nucleic acid sequence via binding of said oligonucleotides with said target nucleic acid sequence] comprising:

a) generating a library of nucleobase sequences *in silico* according to [defined criteria] thermodynamic property, target accessibility, targeting to functional regions of target nucleic acid sequence, or uniform distribution to target nucleic acid sequence, wherein said oligonucleotides modulate the expression of a target nucleic acid sequence via binding of said oligonucleotides with said target nucleic acid sequence;

b) evaluating *in silico* a plurality of virtual oligonucleotides having the nucleobase sequences of a) according to [defined criteria, wherein said defined criteria is] thermodynamic property, target accessibility, targeting to functional regions of target nucleic acid sequence, or uniform distribution to target nucleic acid sequence; and

c) robotically assaying a plurality of synthetic oligonucleotides corresponding to at least some of said virtual oligonucleotides for one or more desired physical, chemical or biological properties.

69.   (Amended) A method of generating a set of oligonucleotides [that modulate the expression of a target nucleic acid sequence via binding of said oligonucleotides with said target nucleic acid sequence] comprising:

a) evaluating *in silico* a plurality of virtual oligonucleotides according to defined criteria, wherein said defined criteria is thermodynamic property, target accessibility, targeting to functional regions of target nucleic acid sequence, or uniform distribution to target nucleic acid sequence;

b) robotically synthesizing a plurality of synthetic oligonucleotides corresponding to at least some of said virtual oligonucleotides; and

c) robotically assaying said plurality of synthetic oligonucleotides for one or more desired physical, chemical or biological properties.

70.   (Amended) A method of generating a set of oligonucleotides [that modulate the expression of a target nucleic acid sequence via binding of said oligonucleotides with said target nucleic acid sequence] comprising:

a) generating a library of nucleobase sequences *in silico* according to [defined criteria] thermodynamic property, target accessibility, targeting to functional regions of target nucleic acid sequence, or uniform distribution to target nucleic acid sequence;

b) evaluating *in silico* a plurality of virtual oligonucleotides having the nucleobase sequences of a) according to [defined criteria, wherein said defined criteria is] thermodynamic property, target accessibility, targeting to functional regions of target nucleic acid sequence, or uniform distribution to target nucleic acid sequence;

c) robotically synthesizing a plurality of synthetic oligonucleotides corresponding to at least some of said virtual oligonucleotides; and

d) robotically assaying said plurality of synthetic oligonucleotides for one or more desired physical, chemical or biological properties.

71.   (Amended) A method of generating a set of oligonucleotides [that modulate the expression of a target nucleic acid sequence via binding of said oligonucleotides with said target nucleic acid sequence,] comprising:

a) generating a library of nucleobase sequences *in silico* according to [defined criteria] thermodynamic property, target accessibility, targeting to functional regions of target nucleic acid sequence, or uniform distribution to target nucleic acid sequence;

b) choosing an oligonucleotide chemistry;

c) evaluating *in silico* a plurality of virtual oligonucleotides having the nucleobase sequences of a) and the oligonucleotide chemistry of b) according to [defined criteria, wherein said defined criteria is] thermodynamic property, target accessibility, targeting to functional regions of target nucleic acid sequence, or uniform distribution to target nucleic acid sequence, and selecting those having preferred characteristics, in order to generate a set of preferred nucleobase sequences;

d) robotically synthesizing a set of synthetic oligonucleotides having said preferred nucleobase sequences of step c) and said oligonucleotide chemistry of step b);

e) robotically assaying said set of synthetic oligonucleotides of step (d) for a physical, chemical or biological activity; and

f) selecting a subset of said set of synthetic oligonucleotides of step d) having a desired level of physical, chemical or biological activity in order to generate said set of oligonucleotides.

72.   (Amended) A method of identifying one or more nucleic acid sequences amenable to antisense binding of an oligonucleotide to said nucleic acid sequences comprising:

evaluating *in silico* a plurality of virtual oligonucleotides according to [defined criteria] thermodynamic property, target accessibility, targeting to functional regions of target nucleic acid sequence, or uniform distribution to target nucleic acid sequence; and

robotically assaying a plurality of synthetic oligonucleotides corresponding to least some of said virtual oligonucleotides for one or more desired physical, chemical or biological properties by computer-controlled [real-time] polymerase chain reaction or by computer-controlled enzyme-linked immunosorbent assay.

74.   (Amended) A method of identifying one or more nucleic acid sequences amenable to antisense binding of an oligonucleotide to said nucleic acid sequences comprising:

generating a library of nucleobase sequences *in silico* according to [defined criteria] thermodynamic property, target accessibility, targeting to functional regions of target nucleic acid sequence, or uniform distribution to target nucleic acid sequence; and

robotically assaying a plurality of synthetic oligonucleotides having said nucleobase sequences for one or more desired physical, chemical or biological properties by computer-controlled [real-time] polymerase chain reaction or by computer-controlled enzyme-linked immunosorbent assay.

75.   (Amended) A method of identifying one or more nucleic acid sequences amenable to antisense binding of an oligonucleotide to said nucleic acid sequences comprising:

a) generating a library of nucleobase sequences *in silico* according to [defined criteria] thermodynamic property, target accessibility, targeting to functional regions of target nucleic acid sequence, or uniform distribution to target nucleic acid sequence;

b) evaluating *in silico* a plurality of virtual oligonucleotides having the nucleobase sequences of a) according to [defined criteria] thermodynamic property, target accessibility, targeting to functional regions of target nucleic acid sequence, or uniform distribution to target nucleic acid sequence; and

c) robotically assaying a plurality of synthetic oligonucleotides corresponding to at least some of said virtual oligonucleotides for one or more desired physical, chemical or biological properties by computer-controlled [real-time] polymerase chain reaction or by computer-controlled enzyme-linked immunosorbent assay.

78.   (Amended) A method of identifying one or more nucleic acid sequences amenable to antisense binding of an oligonucleotide to said nucleic acid sequences comprising:

a) evaluating *in silico* a plurality of virtual oligonucleotides according to [defined criteria, wherein said defined criteria is] thermodynamic property, target accessibility, targeting to functional regions of target nucleic acid sequence, or uniform distribution to target nucleic acid sequence;

b) robotically synthesizing a plurality of synthetic oligonucleotides corresponding to at least some of said virtual oligonucleotides; and

c) robotically assaying said plurality of synthetic oligonucleotides for one or more desired physical, chemical or biological properties.

79.   (Amended) A method of identifying one or more nucleic acid sequences amenable to antisense binding of an oligonucleotide to said nucleic acid sequences comprising:

a) generating a library of nucleobase sequences *in silico* according to [defined criteria] thermodynamic property, target accessibility, targeting to functional regions of target nucleic acid sequence, or uniform distribution to target nucleic acid sequence;

b) evaluating *in silico* a plurality of virtual oligonucleotides having the nucleobase sequences of a) according to [defined criteria, wherein said defined criteria is] thermodynamic property, target accessibility, targeting to functional regions of target nucleic acid sequence, or uniform distribution to target nucleic acid sequence;

c) robotically synthesizing a plurality of synthetic oligonucleotides corresponding to least some of said plurality of virtual oligonucleotides; and

d) robotically assaying said plurality of synthetic oligonucleotides for one or more desired physical, chemical or biological properties.

80.   (Amended) A method of identifying one or more nucleic acid sequences amenable to antisense binding of an oligonucleotide to said nucleic acid sequences comprising:

a) generating a library of nucleobase sequences *in silico* according to [defined criteria] thermodynamic property, target accessibility, targeting to functional regions of target nucleic acid sequence, or uniform distribution to target nucleic acid sequence;

b) choosing an oligonucleotide chemistry;

c) evaluating *in silico* a plurality of virtual oligonucleotides having the nucleobase sequences of a) according to [defined criteria, wherein said defined criteria is] thermodynamic property, target accessibility, targeting to functional regions of target nucleic acid sequence, or uniform distribution to target nucleic acid sequence, and selecting those having preferred characteristics, in order to generate a set of preferred nucleobase sequences;

d) robotically synthesizing a set of synthetic oligonucleotides having said preferred nucleobase sequences of step b) and said oligonucleotide chemistry of step c);

e) robotically assaying said set of synthetic oligonucleotides of step d) for a physical, chemical or biological activity; and

f) selecting a subset of said set of oligonucleotides of step d) having a desired level of physical, chemical or biological activity.

81.   (Amended) A method of identifying one or more nucleic acid sequences amenable to antisense binding of an oligonucleotide to said nucleic acid sequences comprising:

evaluating *in silico* a plurality of virtual oligonucleotides according to [defined criteria, wherein said defined criteria is] thermodynamic property, target accessibility, targeting to functional regions of target nucleic acid sequence, or uniform distribution to target nucleic acid sequence; and

robotically assaying a plurality of synthetic oligonucleotides corresponding to least some of said virtual oligonucleotides for one or more desired physical, chemical or biological properties.

82.   (Amended) A method of identifying one or more nucleic acid sequences amenable to antisense binding of an oligonucleotide to said nucleic acid sequences comprising:

a) generating a library of nucleobase sequences *in silico* according to [defined criteria] thermodynamic property, target accessibility, targeting to functional regions of target nucleic acid sequence, or uniform distribution to target nucleic acid sequence;

b) evaluating *in silico* a plurality of virtual oligonucleotides having the nucleobase sequences of a) according to [defined criteria, wherein said defined criteria is] thermodynamic property, target accessibility, targeting to functional regions of target nucleic acid sequence, or uniform distribution to target nucleic acid sequence; and

c) robotically assaying a plurality of synthetic oligonucleotides corresponding to at least some of said virtual oligonucleotides for one or more desired physical, chemical or biological properties.

85.   (Amended) A method of identifying one or more nucleic acid sequences amenable to antisense binding of an oligonucleotide to said nucleic acid sequences comprising:

a) evaluating *in silico* a plurality of virtual oligonucleotides according to [defined criteria, wherein said defined criteria is] thermodynamic property, target accessibility, targeting to functional regions of target nucleic acid sequence, or uniform distribution to target nucleic acid sequence;

b) robotically synthesizing a plurality of synthetic oligonucleotides corresponding to at least some of said virtual oligonucleotides; and

c) robotically assaying said plurality of synthetic oligonucleotides for one or more desired physical, chemical or biological properties.

86.   (Amended)   A method of identifying one or more nucleic acid sequences amenable to antisense binding of an oligonucleotide to said nucleic acid sequences comprising:

a) generating a library of nucleobase sequences *in silico* according to [defined criteria] thermodynamic property, target accessibility, targeting to functional regions of target nucleic acid sequence, or uniform distribution to target nucleic acid sequence;

b) evaluating *in silico* a plurality of virtual oligonucleotides having the nucleobase sequences of a) according to [defined criteria, wherein said defined criteria is] thermodynamic property, target accessibility, targeting to functional regions of target nucleic acid sequence, or uniform distribution to target nucleic acid sequence;

c) robotically synthesizing a plurality of synthetic oligonucleotides corresponding to least some of said plurality of virtual oligonucleotides; and

d) robotically assaying said plurality of synthetic oligonucleotides for one or more desired physical, chemical or biological properties.

87.   (Amended)   A method of identifying one or more nucleic acid sequences amenable to antisense binding of an oligonucleotide to said nucleic acid sequences comprising:

a) generating a library of nucleobase sequences *in silico* according to [defined criteria] thermodynamic property, target accessibility, targeting to functional regions of target nucleic acid sequence, or uniform distribution to target nucleic acid sequence;

b) choosing an oligonucleotide chemistry;

c) evaluating *in silico* a plurality of virtual oligonucleotides having the nucleobase sequences of a) according to [defined criteria, wherein said defined criteria is] thermodynamic property, target accessibility, targeting to functional regions of target nucleic acid sequence, or uniform distribution

to target nucleic acid sequence, and selecting those having preferred characteristics, in order to generate a set of preferred nucleobase sequences;

d) robotically synthesizing a set of synthetic oligonucleotides having said preferred nucleobase sequences of step b) and said oligonucleotide chemistry of step c);

e) robotically assaying said set of synthetic oligonucleotides of step d) for a physical, chemical or biological activity; and

f) selecting a subset of said set of oligonucleotides of step d) having a desired level of physical, chemical or biological activity.

99.   (Amended) A method of defining a set of compounds [that modulate the expression of a target nucleic acid sequence via binding of said compounds with said target nucleic acid sequence] comprising:

evaluating *in silico* a plurality of virtual compounds according to [defined criteria, wherein said defined criteria is] thermodynamic property, target accessibility, targeting to functional regions of target nucleic acid sequence, or uniform distribution to target nucleic acid sequence; and

robotically synthesizing a plurality of synthetic compounds corresponding to said plurality of virtual compounds.

100.   (Amended) A method of generating a set of oligonucleotides [that modulate the expression of a target nucleic acid sequence via binding of said oligonucleotides with said target nucleic acid sequence] comprising:

a) generating a library of nucleobase sequences *in silico* according to [defined criteria] thermodynamic property, target accessibility, targeting to functional regions of target nucleic acid sequence, or uniform distribution to target nucleic acid sequence;

b) evaluating *in silico* a plurality of virtual oligonucleotides having the nucleobase sequences of a) according to [defined criteria, wherein said defined criteria is] thermodynamic property, target accessibility, targeting to functional regions of target nucleic acid sequence, or uniform distribution to target nucleic acid sequence; and

c) robotically synthesizing a plurality of synthetic oligonucleotides corresponding to at least some of said virtual oligonucleotides.

101.   (Amended) A method of [identifying one or more nucleic acid sequences amenable to antisense binding of an oligonucleotide to said nucleic acid sequences] preparing oligonucleotides comprising:

evaluating *in silico* a plurality of virtual oligonucleotides according to [defined criteria, wherein said defined criteria is] thermodynamic property, target accessibility, targeting to functional regions of target nucleic acid sequence, or uniform distribution to target nucleic acid sequence; and

robotically synthesizing a plurality of synthetic oligonucleotides corresponding to least some of said virtual oligonucleotides.

102.   (Amended) A method of [identifying one or more nucleic acid sequences amenable to antisense binding of an oligonucleotide to said nucleic acid sequences] preparing oligonucleotides comprising:

a) generating a library of nucleobase sequences *in silico* according to [defined criteria] thermodynamic property, target accessibility, targeting to functional regions of target nucleic acid sequence, or uniform distribution to target nucleic acid sequence;

b) evaluating in silico a plurality of virtual oligonucleotides having the nucleobase sequences of a) according to [defined criteria, wherein said defined criteria is] thermodynamic property, target accessibility, targeting to functional regions of target nucleic acid sequence, or uniform distribution to target nucleic acid sequence; and

c) robotically synthesizing a plurality of synthetic oligonucleotides corresponding to at least some of said virtual oligonucleotides.